Fallot's Tetralogy: The Pathological Aspect

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THE general pathologist has, until very recently, shown little interest in congenital malformations of the heart. Apart from a few anomalies thought to be significant in the production and localisation of bacterial endocarditis, most of these anomalies have been encountered by him in new-born infants, or in infants dying within the first six, or, at most, twelve months of life. The lesions have usually been complex and highly variable from case to case, and it has often been difficult to appreciate how the child lived at all. To make a detailed anatomical study of the abnormalities found in early infancy would deter anyone from ever expecting to make an accurate clinical diagnosis. Until Dr. Taussig's work, it may be said that only a few workers appreciated that, among those children surviving beyond the first year of life and showing cyanosis, the great majority suffered from a fundamentally similar defect and showed the four features described by Fallot in 1888 and usually known as the "tetralogy of Fallot."

No sound knowledge of any disease can be obtained without some understanding of its structural basis. Biochemical equations and biophysical concepts may be enough for some, but most of us will feel, as Robert Louis Stevenson said in another context, that these concepts lie in regions where there is no habitable city for the mind of man. Some such apology is necessary for this brief account of the morbid anatomy of the condition.

The condition as described by Fallot consists of four features, hence the name "tetralogy." These are pulmonary stenosis or atresia, dextroposition of the aorta, an interventricular septal defect, and hypertrophy of the right ventricle. These must be discussed separately.

PULMONARY STENOSIS OR ATRESIA

The pulmonary stenosis may affect either the infundibulum of the right ventricle, that is, the portion of the heart representing the bulbis cordis of lower animals, or the pulmonary valve only. Involvement of the infundibulum may vary from what is almost a subdivision of the right ventricle into two halves, with a narrowed orifice between, to a complete, or almost complete, absence of the passage leading to what may be only a fibrous strand representing the pulmonary artery. The difficulty of diagnosis of the site and nature of the obstruction during life must temper enthusiasm for operations directed to the heart or to the valve itself,[2] and especially for all attempts to divide structures blindly in the heart chambers.

When there is a pulmonary atresia and no passage for blood direct from the right ventricle to the lungs, the condition is often called an extreme tetralogy, and the circulation to the lungs depends on blood passing to the pulmonary arteries along the ductus arteriosus and on the bronchial arteries arising from the aorta. The ductus arteriosus undergoes functional closure immediately after birth, and, though it may remain open or re-open temporarily under conditions of extreme

anoxia,[7, 8] it must, if properly developed, undergo permanent organic closure in a few months.[6] In these cases the condition of the bronchial arteries and of the various lung branches from the mediastinal arteries is rarely adequately studied at autopsy. The literature has been reviewed by Christeller (1916).[3] Death in the early months of life is rarely to be attributed only to closure of the ductus arteriosus. The worst cases have the walls of the stenosed infundibulum or the valves so fixed by fibrosis that they cannot expand with the growth of the other blood channels. Some assessment of salvageable material is probably possible at the end of the first year of life.

Dextroposition of the Aorta

The dextroposition of the aorta means that the aorta comes to lie across the outflow from both ventricles, so that it receives blood from both. Though described as a Type I transposition of Spitzer (1923),[11] it is not a true transposition, since the pulmonary artery still arises entirely from the right ventricle and is not transposed to the left ventricle. This dextroposition varies from case to case and is important, since the aperture between the aorta and the left ventricle is really a measure of the volume of oxygenated blood received from the lungs and expelled from the left ventricle into the aorta.

Interventricular Septal Defect

The defect in the upper membranous part of the interventricular septum is the inevitable result of the incomplete dextroposition of the aorta. The formation of the cardiac septa is one of the most difficult subjects in embryology and it is unnecessary to discuss it here.

Hypertrophy of Right Ventricle

The right ventricle is hypertrophied in relation to the heart as a whole and to the left ventricle. This is due to this chamber having to expel the blood derived from the left ventricle and received by the great veins, plus that quantity of blood which it has driven into the aorta instead of into the pulmonary arteries, and which then also returns to it through the systemic veins and the right auricle. It must also expel this blood through the narrowed pulmonary orifice, or at a blood pressure equal to that in the systemic circulation into the aorta.

The functional result of these abnormalities is that only a part of the total blood volume passes through the lungs during each circuit, and a volume of unaltered venous blood, varying from case to case, is passed direct into the systemic circulation. This reduced pulmonary blood-flow is probably responsible for the lesions which develop in the pulmonary arteries and veins. These are well described by Rich (1948).[10] Thrombi, composed in great part of fibrin, form in these vessels and undergo organisation. These thrombi never appear to occlude the entire lumen of a vessel, and they undergo recanalisation. The proportion of vessels affected and the extent of involvement of individual vessels has not been studied, and would require the application of recently discovered techniques. The lesions may never be sufficiently extensive to impede the passage of the small volume of blood passing through the lungs in this condition, but after the circulation has been improved

by the Blalock operation or a similar procedure, and despite the high pulmonary arterial pressure, they might, if very extensive, reduce the flow through the lungs.

Two cases representative of the tetralogy of Fallot have come to autopsy after operation and only these cases will be referred to now.

Case I

This three-year-old child died on the operating table. Only the thoracic contents were made available for examination. The heart showed the usual features: stenosis of the infundibulum was present, but was not excessive, and the aorta did not far over-ride the right ventricle. Projecting into the channel of the narrow passage of the infundibulum were two sessile masses of fibrin about 1 to 2 mm. in diameter, firmly adherent to the thickened, wrinkled, and opaque endocardium. The pulmonary valves were uniformly slightly thickened and the pockets formed by the valve cusps unusually deep, but three cusps were present and there was no fusion along their edges. Detailed histological study showed evidence of older organised fibrin aggregates, and in the more recent lesions only occasional mononuclear cells and fibroblasts at the base of the fibrin vegetation. There were no lesions on any of the heart valves or around the defect in the interventricular septum; the myocardium showed no cellular infiltration; and the endocardium was thin, except in the infundibulum, where there was some slightly irregular lamination of dense fibrous tissue, but little elastic tissue. There is much the same difficulty as Lewis and Grant (1923)[9] experienced in their study of bicuspid aortic valves of congenital and bacterial origin, but it seems probable that the vegetations superimposed on the congenitally malformed infundibulum should be regarded as non-infective. The occurrence of infection in the conus, along with lesions on the tricuspid valve, is described by Harrison (1929)[5] and recorded by Abbott (1936).[1]

Conditions would seem very favourable for the lodgment of bacteria, and, as an increasing number of these cases are enabled to survive into later life, the incidence of bacterial endocarditis should be carefully studied.

This case died on the operating table. During this operation the lung on the side of the operation is collapsed and the child depends on the opposite lung. In this patient the right lung was collapsed. The right pulmonary artery was a wide channel; the left, supplying the lung and functioning alone during the operation, was narrowed just between its origin from the common stem and the position of the ductus arteriosus. Here it would not pass a probe which easily passed the region of stenosis in the infundibulum, and was obviously incapable of sustaining the pulmonary circulation alone. The cause of this infantile co-arctation of the pulmonary artery—if it may be so designated—could not be established. The wall was normal, but the adjacent ductus arteriosus contained a calcified thrombus in a lumen, which was closed at both ends. Structural closure of this structure should not normally be associated with thrombosis, and there may have been some growth dysplasia of these two related structures.

Case II

In the second case there was gross narrowing of the infundibulum, with a fibrous diaphragm marking its junction with the ventricle. A few small vegetations similar

to these in the first case were present on the thickened wall of the infundibulum. There was gross dextroposition of the aorta, and, as well as the high interventricular septal defect, a wide defect in the muscular part of the septum low down permitted much admixture of blood in the ventricles. This must be regarded as a dissociated anomaly. In this case structural changes had closed the ductus arteriosus normally, but large bronchial vessels arising from the aorta were found and must have contributed largely to the blood supply of the lungs. This child survived twenty-four hours after anastomosis of the right cartoid to the upper lobe branch of the right pulmonary artery. Thrombus was forming at the site of the anatomosis and in the blind end of the right subclavian, which was also divided, and it is doubtful if the operation would have been satisfactory.

A peculiar finding in this case was an extensive interstitial myocarditis composed chiefly of mononuclear cells, including Anitschkoiv cells, and a few eosinophils. There was a terminal serous myocarditis, probably the result of terminal circulatory changes, but the cellular process appeared to ante-date the operation. The functional significance of such a myocarditis cannot be assessed, nor can any suggestions be offered as to its ætiology, and it is doubtful if any refinement of clinical examination could reveal its presence. In this case death was largely due to the failure to relieve sufficiently the gross degree of infundibular stenosis.

While the Blalock operation and its variants represent a very great advance in surgery, it is not, and cannot be, the final answer to this anomaly. Modern blood-vessel and cardiac surgery is largely the product of experimental surgery in animals. Operations such as the Blalock procedure and the operations for patent ductus arteriosus and coarctation of the aorta were devised by surgeons trained in the experimental tradition. In the laboratories of experimental surgery the search for a new approach to this problem is being continued. Advances which have been made suggest that real progress in surgery requires, first, a thorough understanding of the disease process, and then well conducted animal experiments.

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